Challenges in understanding the role of pregnancy morbidity in cardiovascular risk in SLE

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Cardiovascular disease (CVD) is a leading cause of morbidity and mortality in systemic lupus erythematosus (SLE). Despite extensive and ongoing research in this area, few risk factors, including traditional ones such as smoking and hypertension, explain a significant proportion of the risk. There is a robust scientific literature showing that the prevalence of cardiovascular risk factors such as endothelial dysfunction, hypertension and increased arterial stiffness increase after pre-eclampsia, as do future risks of metabolic syndrome and CVD.

Given that a majority of patients with SLE are women of reproductive age and the reported early CVD morbidity in women with SLE, investigating the relationship between pre-eclampsia (and other pregnancy complications) and subsequent CVD risk is of great interest in SLE. To that end, investigators explored the link between pregnancy complications and subsequent CVD using cross-sectional data from 129 women with systemic lupus in this issue.

Despite their clear question and the clinical significance, the study design and available data only hint at an answer. Although complications such as pre-eclampsia have been shown to be more common in SLE pregnancies compared with the general population, these are still relatively rare complications. Coupled together with a relatively uncommon disease (SLE), the study lacks the statistical power to make definitive conclusions and cannot fully account for potential confounders. However, the authors should be commended for accumulating the number of patients they did. This work should be viewed as exploratory, building a scientific foundation for more definitive studies that can unravel the relationship between SLE, pregnancy morbidity and subsequent CVD risk.

Should pregnancy complications alert clinicians caring for women with SLE about subsequent CVD risks necessitating more aggressive risk factor modification? Should pre-eclampsia be viewed as a ‘failed cardiac stress test’? And lastly, does the presence of SLE and pre-eclampsia together substantially increase CVD risk, greater than would be expected with either risk factor alone? Lin and Ramsey-Goldman et al’s discussion naturally begs each of these questions. To build upon the foundation of this work and assess these issues, some design, data collection and analytical considerations will need to be accounted for in future studies. It would be of interest to examine different pregnancy complications separately, since pre-eclampsia may confer a different risk than outcomes such as having an infant with low birth weight. Also, more fully exploring the timing of pre-eclampsia in relation to SLE diagnosis would be of interest, since presence of both conditions during pregnancy might confer a higher risk. It is important to note that the majority of patients (two-thirds) in Lin and Ramsey-Goldman’s study experienced pre-eclampsia before a diagnosis of SLE. It remains unclear how much time between pregnancy and CVD assessment and risk factor modification is needed, and whether the presence of other modifiable risk factors should change current screening and treatment practices. In addition, it would be interesting to understand how multiple pregnancies and multiple gestations influence these relationships.

As the body of evidence between CVD and pregnancy morbidity grows, this line of study may unlock key risk factors to aid in the identification and management of early CVD in women with SLE. To answer the clinical questions posed here and by the authors and to overcome the methodological challenges, there is a need for robust, longitudinal, clinically rich, population-based data.

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